

This dramatic but rare fatal complication of mitral valve disease should not be dismissed as a mere academic curiosity. With increasing use of slow-release potassium tablets it may become more common. One of the patients described by Whitney and Croxon died of gastrointestinal haemorrhage and two of their patients had sufficient dysphagia to need feeding jejunostomies. In view of all this it seems desirable to use effervescent potassium chloride or potassium chloride mixture rather than potassium chloride tablets in patients with chronic mitral valve disease complicated by left atrial dilation.

¹ Ashby, W B, Humphreys, J, and Smith, S J, *British Medical Journal*, 1965, **2**, 1409.

² Wynn, V, *British Medical Journal*, 1965, **2**, 1546.

³ Pemberton, J, *British Heart Journal*, 1970, **32**, 267.

⁴ Whitney, B, and Croxon, R, *Clinical Radiology*, 1972, **23**, 147.

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Placental and mammary transfer of sulphasalazine

Sulphasalazine (SASP) is widely used as maintenance treatment for ulcerative colitis. Since many of the patients are women in the reproductive age there is the question of the extent to which the drug and its metabolites reach the fetus, and also to what extent they are present in the milk if the treatment is continued throughout pregnancy and the period of lactation. SASP consists of sulphapyridine linked to a salicylate radical by a diazo bond. When taken by mouth only a limited amount is absorbed from the small intestine and most of the drug reaches the colon intact. There it is split at the diazo bond by the colonic bacteria into sulphapyridine (SP) and 5-aminosalicylic acid (5-ASA). The SP is virtually all absorbed and is then metabolised in the usual way of sulphonamides. The 5-ASA is only partly absorbed and is rapidly excreted in the urine so that the serum concentration is very low.¹⁻² There is strong evidence that virtually all the complications of SASP therapy are attributable to its SP component.

Patients, methods, and results

Five patients with ulcerative colitis who became pregnant while on maintenance treatment with SASP volunteered to take part in the study, which merely required them to allow additional samples of blood and a sample of milk to be taken for analysis. As is our usual practice, they were continued on SASP in a dose of 0.5 g four times a day throughout their

Concentrations of SASP and its metabolites in maternal sera and in corresponding cord sera, amniotic fluid, and breast milk. Values are expressed in µg/ml (mean ± SD)

	Results in 5 cases			Results in 3 cases	
	Maternal serum	Cord serum	Amniotic serum	Maternal serum	Breast milk
SASP	7.3 ± 4.0	4.2 ± 3.0	0.6 ± 0.5	8.8 ± 1.9	2.7 ± 1.8
Total-SP ..	10.6 ± 4.6	11.0 ± 4.0	16.0 ± 8.9	19.0 ± 3.1	10.3 ± 1.6
Free-SP ..	6.7 ± 4.1	4.6 ± 3.0	8.6 ± 5.6	13.8 ± 4.0	6.5 ± 2.2
SP-Gluc ..	0.0	0.4 ± 0.2	0.6 ± 0.9	0.1 ± 0.2	1.6 ± 2.8
Ac-SP ..	3.7 ± 2.4	4.9 ± 1.8	4.8 ± 3.4	4.5 ± 2.3	1.4 ± 0.7
Ac-SP Gluc ..	0.5 ± 0.3	0.6 ± 0.5	1.9 ± 0.7	0.6 ± 0.4	0.8 ± 1.0
Total 5-ASA ..	<0.5	<0.5	1.2 ± 0.5	Not measured	Not measured

pregnancy and puerperium. Samples of maternal and cord blood and amniotic fluid were collected at the time of delivery. In three of the patients who proceeded to breast-feeding samples of maternal blood and milk were collected one week after delivery. The standard chemical methods³⁻⁵ were used to estimate SASP; SP; N⁴-acetyl-sulphapyridine-O-glucuronide (Ac-SP-Gluc); total-sulphapyridine (total-SP), which represents SP and all its metabolites; and total-5-ASA (free 5-ASA plus acetyl-5-ASA).

The table shows that SASP crosses the placenta, the mean concentration in the cord serum being half that of the maternal serum. The concentration of SASP in the amniotic fluid was very low. The concentrations of total-SP were identical in the maternal and cord sera. The concentrations of free-SP, however, were significantly lower ($P < 0.02$) and those of total acetylated sulphapyridine (Ac-SP + Ac-SP-Gluc) were significantly higher ($P < 0.025$) in the cord sera than in the maternal sera. There was no detectable SP-Gluc in the maternal sera but low concentrations were found in the cord sera. The concentrations of total-5-ASA were very low in all types of fluid examined.

Both SASP and SP pass into breast milk. The SASP concentration in the milk was about 30% of that in the maternal serum, while the mean total-SP concentration in the milk was about 50% of that of maternal serum. The various metabolites of SP were present in the milk in roughly the same proportions as in the maternal serum. 5-ASA was not measured in the milk since no satisfactory analytical method was available, but it is likely to be very low as only low serum concentrations are ever found in patients receiving SASP therapy, being 1.0 ± 0.7 µg/ml in our own patients on a dose of 2 g daily.

Comment

Sulphasalazine has been used extensively during pregnancy and no untoward effect on its course or on the fetus has been reported. Our clinical experience at Oxford agrees with this finding. It has been our usual practice for the past 10 years to continue maintenance therapy with SASP throughout pregnancy and the puerperium in patients with ulcerative colitis and we have seen no obvious ill effects on the mother or the child. Nevertheless, this study shows that SASP and its metabolites reach the fetus in concentrations not greatly different from those in the maternal serum. There is therefore a theoretical risk that the fetus might develop complications from the treatment. The concentrations of SASP and its metabolites in breast milk are much lower than those of maternal serum and are unlikely to cause harmful side effects.

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¹ Schroder, H, and Campbell, D E S, *Clinical Pharmacology and Therapeutics*, 1972, **13**, 539.

² Peppercorn, M A, and Goldman, P, *Gastroenterology*, 1973, **64**, 240.

³ Hansson, K-A, and Sandberg, M, *Acta Pharmaceutica Suecica*, 1973, **10**, 87.

⁴ Sandberg, M, and Hansson, K-A, *Acta Pharmaceutica Suecica*, 1973, **10**, 107.

⁵ Hansson, K-A, *Acta Pharmaceutica Suecica*, 1973, **10**, 153.

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Collapse after oral disopyramide

Disopyramide is electrophysiologically similar to quinidine and has been used to treat supraventricular and ventricular arrhythmias since the late 1960s.¹ Absorption of the oral dose is rapid and almost complete with peak serum concentrations at one to two hours. In five of our patients disopyramide by mouth was followed by severe myocardial depression, hypotension, a rise in venous pressure, and, in four, unexplained severe abdominal pain (table). The following two cases are representative.

Case reports

(1) A 67-year-old man who had had myocardial infarctions developed profound hypotension, sudden severe epigastric pain, dyspnoea, sweating, and raised jugular venous pressure (JVP) after being given disopyramide 400 mg by mouth to revert paroxysmal atrial flutter. He was treated with metaraminol, isoprenaline, and frusemide. Pulmonary embolus was